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Modern Concepts of Cardiovascular Disease

Published monthly by the AMERICAN HEART ASSOCIATION
44 EAST 23RD STREET, NEW YORK 10, N. Y.

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FEB 17 1956

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Vol. XXV JANUARY, 1956 No. 1

THE LIVER IN CONGESTIVE HEART FAILURE*

The status of the liver in congestive heart failure may be briefly summarized. The role of hepatic congestion as a producer of symptoms and a valuable diagnostic physical finding is well known. In congestive heart failure there occurs a clearly defined pattern of histological changes in the liver, culminating at times in "cardiac fibrosis." These marked anatomical changes are accompanied by multiple alterations in the common liver function tests, but surprisingly are seldom the cause of direct clinical manifestations in terms of insufficiency of hepatic functions as we now recognize them. With advancing knowledge of the more obscure aspects of liver function, and of the physiology of salt retention, it is likely that the role of hepatic disturbance in the pathophysiology of congestive heart failure will assume increasing importance.

Symptoms and Signs

A patient whose only urgent complaint is right upper quadrant pain can be relieved when early right heart failure is recognized and treated. Such pain may be misconstrued as due to gall bladder disease or hepatitis. An important clue to the correct diagnosis of hepatic congestion is a history of pain increasing with exertion. On the other hand, either cholecystitis or hepatitis may occur in a patient with heart disease. This possibility should not be discarded too lightly, particularly if fever is present. Hepatic enlargement may appear as the first clear evidence of congestive heart failure and may persist for weeks or months after other signs of congestion have disappeared. An enlarged tender liver is therefore occasionally found even though the antecubital venous pressure is normal at rest. Nevertheless, such patients can often be demonstrated to have an elevated venous pressure during exercise.

An enlarged liver is one of the valuable physical signs supporting a diagnosis of congestive heart failure, but caution is necessary here as in all judgments based on a presumption of liver enlargement. A palpable liver is not necessarily enlarged since the position of the upper border must be taken into consideration. More valuable than enlargement alone is the observation of *changes* in size of the liver between examinations (an observation abetted by clear recording of measurements in centimeters), or the finding of definite hepatic tenderness.

A true systolic expansile pulsation of the liver is, of course, an important sign of tricuspid valve insufficiency.

The hepato-jugular reflex as an indication of hepatic congestion is not thoroughly reliable because filling of the neck veins may result from changes in the patient's respirations when the liver is being compressed.

The anorexia and weight loss of congestive heart failure may prove as much due to liver impairment as to disturbed function of the gastrointestinal tract.

Anatomical Changes

The anatomical changes in the liver which accompany congestive heart failure are strikingly uniform. There is still debate concerning the pathogenesis of these changes, and the nature of the fibrosis which becomes prominent in prolonged congestive heart failure; but there is no question that the following anatomical changes occur:

1. *Dilatation of the sinusoids and narrowing of the liver cords in the central areas of the lobules.* This has been ascribed to increased venous pressure with subsequent compression of the liver cells; but it seems probable that there is also an atrophy of the liver cells due primarily to anoxia which leads to secondary widening of the sinusoids. Rich[1] has pointed out that a similar picture of widened sinusoids is seen, and often mis-labelled as congestion, in patients with severe anemia even though no other organs show evidence of passive congestion.

2. *Necrosis of central cells.* This is occasionally extreme, and is probably the chief cause of clinical jaundice when the latter occurs in congestive heart failure *without* concomitant pulmonary infarction. When central necrosis is extensive it leads to confluence of central areas which produced pseudo-lobulation with portal areas at the center of the pseudolobules, surrounded by a rim of surviving liver cells.

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It is notable, as Moschcowitz[2] has pointed out, that the liver is the only organ in which cell necrosis results from circulatory failure in the absence of emboli, thrombosis, or infection. It is suggested that this is because the liver is the only organ in the body which is supplied predominantly by venous blood.

3. *Condensation of reticulum in the degenerated central areas.* Difficulty in distinguishing this from "true cirrhosis" (interpreted as meaning an active proliferation of fibroblasts) has accounted for some of the discrepancies in statistics regarding the incidence of "cardiac cirrhosis."

4. *Marked thickening of the walls of the central veins and hepatic veins.*

5. *Fibrosis of the liver, with active fibroblast proliferation.* That this occurs is clear; but its pathogenesis is not. When it occurs in the central areas it is characteristic of congestive heart failure (or other factors causing a similar prolonged elevation of hepatic venous pressure; but statistical studies have shown that patients with congestive heart failure have an increased incidence of fibrosis in the portal areas as well, either in conjunction with central fibrosis or occurring in the portal areas alone.[3] By some the portal fibrosis has been thought to be indistinguishable from that of Laennec cirrhosis; but Moschcowitz[2] has presented a convincing study (of a small number of patients) suggesting that these fibrotic changes are concomitants of vascular changes which take place subsequent to liver congestion and necrosis.

Liver Function Tests

Impaired liver function, as measured by usual liver function tests, is present in most patients with congestive heart failure.[4]

The major factor accounting for liver damage in congestive heart failure appears to be anoxia of the liver cells. Evidence supporting this view includes:

1. The liver is notably vulnerable to anoxia. For example, atrophy of the liver cords in the central areas is found in patients with prolonged anemias; and necrosis of liver cells develops in dogs kept in a low-oxygen atmosphere.

2. Hepatic blood flow is markedly reduced in congestive heart failure.

3. The centrilobular location of the liver cell damage in congestive heart failure argues strongly for this view. Blood supply to the liver is chiefly venous at its entrance; and the cells nearest the portal areas have first demand on its oxygen content. Simple "compression" by increased venous pressure, on the other hand, should affect the liver cords equally throughout their length.

The impaired liver function resulting from congestive heart failure is reflected in the following tests:

Bromsulfalein Test The test most regularly and markedly disturbed is that of bromsulfalein excretion. This is so consistent a feature of congestive heart failure that it is of diagnostic value in borderline cases. The possible presence of other liver disease (for example, Laennec cirrhosis or hepatitis) must, of course, be kept in mind. Bromsulfalein excretion is sharply affected by decrease in hepatic blood flow. This, as well as cellular malfunction, accounts for the high incidence of delayed bromsulfalein excretion in congestive heart failure.

Serum Bilirubin An elevated serum bilirubin is perhaps the next most common indication of liver dysfunction in congestive heart failure. Often this finding points to the presence of pulmonary infarction, with increased bilirubin production from the infarcted area; but jaundice occurs also in patients with congestive heart failure who at subsequent autopsy have no evidence of infarction in any area. Usually such patients show a striking degree of centrilobular hepatic necrosis. Decreased hepatic blood flow is probably less important in causing jaundice in patients with congestive heart failure than are the factors of: hypoxic depression of liver cells, liver cell necrosis, and increased bilirubin production in infarcted tissues.

Alkaline Phosphatase The alkaline phosphatase is elevated in about half of patients with congestive heart failure and may reach levels of 10 to 14 Bodansky units per cent. The chief importance of this fact is that it should not be allowed to cause diagnostic confusion.

The same is true of the thymol turbidity and cephalin flocculation tests, which are abnormal in about 20 to 30% of patients.

Serum albumin levels are often below normal; but here poor nutrition may be an important factor.

Clinical Manifestions of Impaired Liver Function

Definite clinical manifestations of impaired liver function in congestive heart failure are notable for their rarity (at least as seen by our present dim vision). Dicoumarol hypersensitivity due to impaired prothrombin production has been well documented in occasional patients, but is not common. The presence of increased amounts of antidiuretic factors (including aldosterone) in the urine of congestive heart failure patients may be related to a disorder of metabolism of these substances in the liver—just as it has been shown that estrogen inactivation fails in patients with Laennec cirrhosis. Metabolism of many drugs depends primarily on the liver. The fact that administration of ammonium chloride can precipitate "hepatic coma" in patients with impaired liver function should be kept in mind whenever unusual symptoms appear in a patient being treated with this drug. Dr. Shorr's studies of the VDM and VEM have suggested a relation between vascular reactions and liver function. This perhaps fits together with the observation that patients with Laennec cirrhosis rarely have arterial hypertension. The low blood sedimentation rate which is frequent in congestive heart failure (despite, for example, the presence of active

rheumatic fever) reflects altered serum proteins. The obscure relationship between the liver and the kidney which has given rise to the term hepatorenal syndrome may be of importance in congestive heart failure. Such observations are sufficiently provocative to encourage further study of the extent to which liver impairment adds to over-all disability from heart failure. For the present, it is reasonable to make particular effort to maintain adequate nutrition (especially protein intake) in patients with congestive heart failure in the hope that this will lessen the degree of associated liver damage. Anorexia resulting from congestion and medicines, weight reduction programs, and salt restriction all tend toward poor nutrition of the cardiac patient unless meticulous attention is given to providing an attractive well balanced diet—often best divided into four to six small meals.

Cardiac Cirrhosis

Damage to the liver in congestive heart failure was first recognized in terms of gross and microscopic anatomy. There is no doubt that prolonged congestive heart failure leads to fibrosis of the liver. Applying to this fibrosis the term "cardiac cirrhosis" carries the suggestion that it may lead to clinical effects such as are seen in Laennec cirrhosis—particularly ascites or hepatic failure. Actually, death from hepatic failure is almost never a sequel of congestive heart failure, and ascites in congestive heart failure appears to occur almost as readily without concomitant hepatic fibrosis as with it. However, there are occasional patients in whom the portal hypertension and hypoalbuminemia of "cardiac cirrhosis" contribute to intractable ascites. In such patients abdominal paracentesis may be dramatically helpful, possibly because of improved renal function after relief of the intra-abdominal pressure.

One may suspect cardiac fibrosis of the liver in the presence of prolonged congestive heart failure with marked elevation of venous pressure, predominant ascites, a non-palpable liver, and an enlarged spleen, but the clinical diagnosis of cardiac fibrosis of the liver is notably inaccurate. The liver function tests are of little help in this regard. They tend to be slightly more abnormal in patients who prove to have cardiac fibrosis of the liver, but not in any diagnostic degree or pattern. Congestive heart failure which has produced hepatic fibrosis is generally so severe that the circulatory failure itself dominates the clinical picture.

A question to be answered in the future is whether such "cirrhosis" may progress even after congestive heart failure has been relieved, for example, by valvular surgery. This is possible inasmuch as constriction of circulation by existing fibrotic areas may be a factor in the progression of cirrhosis.

Summary

The symptoms and signs of liver swelling are of known value in the diagnosis of congestive heart failure and in following its course. Right upper quadrant pain may lead to confusion when it is the first symptom of heart failure, particularly since liver swelling may occur when the antecubital venous pressure is normal at rest. Increase in pain or elevation of venous pressure during exercise are helpful clues in making the correct diagnosis.

Characteristic anatomical changes in the liver occur in congestive heart failure ranging from atrophy of the liver cords to diffuse hepatic fibrosis. The occurrence of fibrosis is unquestionable but it does not cause hepatic failure in the sense that this is seen as the terminal phase of other types of cirrhosis.

Liver function tests are extensively altered in congestive heart failure. Clinical consequences of hepatic dysfunction are at present seldom recognized, but will probably become more evident as knowledge of liver metabolism (for example, of enzymes and of antidiuretic substances) advances. For this reason every effort should be made to maintain adequate nutrition in cardiac patients in order to minimize liver impairment.

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The opinions and conclusions expressed herein are those of the author and do not necessarily represent the official views of the Scientific Council of the American Heart Association.

ABSTRACTS OF PAPERS

for

THE 29th ANNUAL SCIENTIFIC SESSIONS,

AMERICAN HEART ASSOCIATION

The 29th Annual Scientific Sessions of the American Heart Association will be held in Cincinnati, Ohio, October 27, 28, 29, 1956 in conjunction with the Association's Annual Meeting. Those interested in presenting papers must submit their abstracts by *May 15.* Abstracts will be accepted only on forms which may be obtained from the Medical Director, American Heart Association, 44 East 23rd Street, New York 10, New York.

Papers intended for presentation should be based on original investigations in or related to the cardiovascular field. The abstracts must be 300 words or less and should contain in summary form the results obtained and the conclusions reached. Abstracts must be submitted in triplicate.

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